

Abstract

GlcNAc-Mal Inhibition of FosB

Antibiotics are used for the treatment of bacterial infections. Fosfomycin, marketed under the name Monurol®, is an antibiotic currently used in the United States to treat urinary tract infections; it can also be used for the treatment of multi-drug-resistant infections. FosB is a fosfomycin resistance enzyme found in Gram-positive organisms, such as methicillin-resistant *Staphylococcus aureus* (MRSA), that if inhibited could lead to better fosfomycin effectiveness. Previous, unpublished research found that N-acetylglucosamine-malate (GlcNAc-Mal) may inhibit the FosB catalyzed nucleophilic addition of bacillithiol (BSH) to fosfomycin, which inactivates the antibiotic. The current study investigates if GlcNAc-Mal can bind to the active site of FosB and act as an inhibitor. A derivatization method was developed that allows the analysis of products using high performance liquid chromatography (HPLC) with UV detection. Standard curve data for the amino acid cysteine, one possible reactant of the reaction, was collected. Experiments explored the inhibition of full enzymatic reactions, to ultimately determine if GlcNAc-Mal is able to inhibit FosB. It is expected that GlcNAc-Mal inhibits FosB by mixed inhibition. A better understanding of how these antibiotic resistant enzymes can be inhibited will lead to a better design of future antibiotics.